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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,412	10/03/2001	Allan Asp	Pha-1626	2742

7590 01/10/2003

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EXAMINER
JOHANNSEN, DIANA B

ART UNIT	PAPER NUMBER
1634	9

DATE MAILED: 01/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/970,412	ASP ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/068,783* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL REJECTION

1. This action is in response to paper no. 8 filed October 15, 2002. Claims 11-12 have been amended and are now pending. The amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

3. Claims 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Apple (WO92/10589; 6/92), for the reasons set forth below and in the Office action of paper no. 6.

Apple teaches methods for amplifying and typing HLA DRbeta genes, and teaches kits comprising reagents that may be employed in his methods (p. 7-8; p. 45-50). Apple's kits comprise solid supports and primers that may be labeled or unlabeled (p. 7). Apple teaches the use of primer pairs wherein one or both primers are biotinylated (p. 34-37, especially p. 36, lines 17-20); Apple therefore teaches primers that are "differently labelled", as well as pairs of primers "comprising one member of a specific binding pair" wherein the member is identical on each of the two primers in the pair. With respect to claim 12, Apple discloses the use of filters and a dot blot manifold (p. 25). With respect to the recitation in the claims of the language "sequencing primers", the mere designation of primers as "sequencing primers" does not further limit

the primers with respect to structure or function; any primer may be employed in some manner in a method of sequencing. It is an inherent property of the primers of Apple that they could be employed in sequencing. It is also noted that Apple teaches that sequencing may be employed in analysis of HLA DRbeta genes (p. 7, p. 24).

The response traverses the rejection on the following grounds. The response argues that "the Examiner is misapplying the teachings of Apple." The response states that "Applicants concede that kits taught by the Apple reference comprise solid supports and primers; however, there is no disclosure, nor even any suggestion, of the inclusion of both amplification and sequencing primers as required in the claims." The response argues that "while there is a discussion of sequencing, the instant claims specifically require that both amplification and sequencing primers be present."

These arguments have been thoroughly considered but are not convincing for the following reasons. The instant claims are drawn not, e.g., to a method requiring steps of amplification and sequencing in which different primers are employed, but rather to a kit that includes "two amplification primers" and "sequencing primers." The mere designation of primers as "sequencing primers" does not limit the structural or functional properties of the claimed primers in a way that would obviate the instant rejection. For example, the instant claims are not limited to particular "amplification primers" that possess either structural or functional properties that would render them unsuitable for use in sequencing. It is well known to those of ordinary skill in the art that amplification primers are routinely employed in sequencing; while such primers would be designated "amplification primers" when employed in amplification and "sequencing

primers" when employed in sequencing, the primers themselves are identical molecules. Further, Applicants have not asserted, or provided any evidence or arguments to support an assertion, that the primers of Apple would not function in methods of nucleic acid sequencing. As discussed in the Office action of paper no. 6, and absent evidence to the contrary, it is an inherent property of the primers of Apple that they could be employed in sequencing, and that they therefore constitute "sequencing primers."

Apple teaches all the limitations recited in present claims 11-12, and therefore this rejection is maintained.

4. Claim 11 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Soderland (EP 371437 A2; 6/90), for the reasons set forth below and in the Office action of paper no. 6.

Soderland teaches methods for analysis of a nucleic acid sequence comprising PCR to produce a "DNA sample in which at least one attachment moiety has been introduced into at least one strand of specific target polynucleotide", attachment of target to a "solid matrix coated with an attachment site to which the attachment moiety or a modification thereof can bind", and determination of the sequence of the amplified target by a method such as the chain termination method (col 2, line 30-col 3, line 31). The affinity pairs used for attachment of target to solid support may include "biotin/avidin or streptavidin" and "hapten/antibody" (col 5, lines 36-45). While Soderland states that, in embodiments employing two modified primers, "The primers must in this case be modified with different attachment moieties", Soderland's teachings encompass the use

of two different moieties that are "of the same type" (e.g., two different haptens with two different antibodies) (col 5, lines 1-4). Soderland teaches that sequencing primers "may be distinct from or equal to the primer used" in amplification, teaches the use of one or "two different sequencing primers", and teaches a variety of different labels for use in sequencing primers, including fluorescent labels (col 8, line 55-col 9, line 46). Soderland discloses that "Reagents for use in practising the method of invention may be packaged in kit form", including amplification primers with "attachment moieties and the corresponding solid supports" and sequencing primers (col 10, line 52-col 11, line 15). With respect to the language "the member being of the same type for both primers", it is noted that Soderland teaches the use together of primers "of the same type", as discussed above.

The response traverses the rejection on the following grounds. The response argues that "the Examiner is mischaracterizing the reference." The response argues that "Soderland teaches that in embodiments employing two modified primers, the primers must be modified with different attachment moieties," and that "such is distinct from the instant claims, which recite that the member (of the specific binding pair) attached to the two amplification primers must be the 'same type for both primers.'" The response further states that the "member must be part of a specific binding pair permitting attachment to the support."

These arguments have been thoroughly considered but are not persuasive for the following reasons. First, Applicants are referred to the Office action of paper no. 6, which stated:

> While Soderland states that, in embodiments employing two modified primers, "The primers must in this case be modified with different attachment moieties", Soderland's teachings encompass the use of two different moieties that are "of the same type" (e.g., two different haptens with two different antibodies) (col 5, lines 1-4).

Second, it is noted that the instant claim is not drawn to methods in which, e.g., a primer pair having particular characteristics is employed, but rather is drawn to a kit "comprising" a support, "two amplification primers," and "sequencing primers." The open transitional language "comprising" permits the inclusion of any number and type of additional reagents (including additional primers) in the claimed kit. Further, the language "two amplification primers" of (b) does not limit the claimed kit to a pair of primers that are employed together, but rather encompasses, e.g., two forward primers, two reverse primers, etc., from different primer pairs. Third, the claim as written is also sufficiently broad so as to encompass two or more copies of the same amplification primer. Specifically, the recitation "two amplification primers comprising one member of a specific binding pair, the member being of the same type for both primers" does not require that the "two amplification primers" be different molecules, and therefore encompasses two of the same molecule, while the open transitional language "comprising" allows for the inclusion of any number of additional reagents, including primers, in the claimed kit. Finally, regarding Applicants statement that the "member must be part of a specific binding pair permitting attachment to the support," it is noted that the instant claim includes no such requirement. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Soderland teaches all the limitations recited in present claim 11, and therefore this rejection is maintained.

Claim Rejections - 35 USC § 103

5. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Soderland (EP 371437 A2; 6/90) in view of Landegren (WO94/11529; 5/94), for the reasons set forth below and in the Office action of paper no. 6.

Soderland teaches methods for analysis of a nucleic acid sequence comprising PCR to produce a "DNA sample in which at least one attachment moiety has been introduced into at least one strand of specific target polynucleotide", attachment of target to a "solid matrix coated with an attachment site to which the attachment moiety or a modification thereof can bind", and determination of the sequence of the amplified target by a method such as the chain termination method (col 2, line 30-col 3, line 31). The affinity pairs used for attachment of target to solid support may include "biotin/avidin or streptavidin" and "hapten/antibody" (col 5, lines 36-45). While Soderland states that, in embodiments employing two modified primers, "The primers must in this case be modified with different attachment moieties", Soderland's teachings encompass the use of two different moieties that are "of the same type" (e.g., two different haptens with two different antibodies) (col 5, lines 1-4). Soderland teaches that sequencing primers "may be distinct from or equal to the primer used" in amplification, teaches the use of one or "two different sequencing primers", and teaches a variety of different labels for use in sequencing primers, including fluorescent labels (col 8, line 55-col 9, line 46). Soderland discloses that "Reagents for use in practising the method of invention may be

packaged in kit form", including amplification primers with "attachment moieties and the corresponding solid supports" and sequencing primers (col 10, line 52-col 11, line 15).

While Soderland teaches the use in his method and kits of a variety of different solid supports (microparticles, test tube, dipsticks, filters, microtitration wells), and states that "The solid matrix can be of any format" (col 7, lines 4-20), Soderland does not disclose the use of a manifold "having a plurality of individual solid phase members" as a solid support, or teach solid phase members "adapted for cooperation with a corresponding set of receptacles", as required by the instant claim. Landegren teaches the use in nucleic acid sequencing of a solid support comprising a manifold having "a plurality of individual solid phase members adapted for cooperation with a corresponding set or sets of receptacles" (p. 3). Landegren discloses that the use of a multipronged manifold solid support permits one to obviate "several of the problems related to the use of separate solid phase elements, like paramagnetic beads or microtiter wells" (p. 2) while facilitating release and transfer of reaction products (p. 2-3). In view of the teachings of Landegren, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Soderland so as to have included in Soderland's kits the manifold solid support of Landegren. An ordinary artisan would have been motivated to have made such a modification in order to have provided practitioners with all the reagents needed for rapid, simultaneous sequencing of several samples using small quantities of reagents, for the advantages of efficiency and cost-effectiveness. With respect to the

language "the member being of the same type for both primers", it is again noted that Soderland teaches the use together of primers "of the same type", as discussed above.

The response traverses the rejection on the following grounds. The response argues that "the claims, as written, do require two amplification primers which comprise one member of a specific binding pair, the member being the same type for both primer," and that "Such is neither disclosed nor even suggested by Landegren, which states that they must be different."

This argument has been thoroughly considered but is not convincing for the following reasons. First, as discussed in the Office action of paper no. 6 and in paragraph 4, above, the Soderland reference, not the Landegren reference, teaches primers meeting the limitations of the claim. The Office action of paper no. 6 clearly indicated that the Landegren reference was cited not for a teaching of any type of primers, but for its teaching of a particular type of solid support (see pages 8-9 of the Office action of paper no. 6). As discussed in the Office action of paper no. 6, an ordinary artisan would have been motivated to have modified the kits of Soderland so as to have included therein the solid support manifold of Landegren in order to have provided practitioners with all the reagents needed for rapid, simultaneous sequencing of several samples using small quantities of reagents, for the advantages of efficiency and cost-effectiveness. Thus, Applicants' argument that Landegren does not teach primers meeting the requirements of the claim is not persuasive with regard to the instant rejection. The response addresses the Landegren reference, but does not address the instant rejection, which relies on the combined teachings of Soderland and

Landegren, as discussed above and in paper no. 6. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The combined references of Soderland and Landegren suggest all the limitations of present claim 12, and therefore this rejection is maintained.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/872-9306 for regular communications and 703/872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana B. Johannsen
January 7, 2003

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600